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V.

ON CHRONIC ARSENICAL POISONING FROM WALL PAPERS AND FABRICS.

By Charles Robert Sanger.

Received November 9, 1893.

During the spring of 1886, while assistant in the Harvard Laboratory, several cases of chronic arsenical poisoning from wall papers were brought to my notice, as the suspected papers and fabrics were sent to me for analysis. In many cases an examination of the urine for arsenic was made, this being done under the supposition that the elimination of arsenic in cases of chronic poisoning had been well studied. I was surprised to find, however, that analyses of the urine in such cases had been comparatively rare, and that little or nothing was known at that time of the elimination of arsenic under the conditions of chronic poisoning from wall papers.

Some of the results of my work were read, by invitation, at a meeting of the South Middlesex (Massachusetts) Society for Medical Improvement in the summer of 1886, but were not published, as so much reference and analytical work remained to be done before the paper could be presented in proper form. I was then called from Cambridge, and for three or four years the completion of the paper was continually prevented by other duties. In the mean time the analysis of the urine became recognized as a necessary step in the diagnosis of chronic arsenical poisoning from wall papers, and the records of such analyses have been frequent, chief among them being the paper of Putnam,* in March, 1889. In nine of the cases cited in this article the analyses had been made by me, and were sent to Dr. Putnam at his request.

Although so much time has elapsed since my work was undertaken, and the cases, as far as the actual poisoning goes, are merely additions to the already long list, yet many facts brought out during the preparation of the paper make it still worthy of publication. Two years ago

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* Bost. Med. Surg. Journ., CXX. 235.

I was about to present the results I had so far obtained, as my negative experiments on the decomposition of arsenical organic matter by mould had enabled me, as I thought, to suggest a possible explanation of the source of wall paper poisoning, if we had to rely on arsenical dust alone as a mode of causation.

The same reasons that led to my postponing the publication of that paper have delayed the appearance of this, and the later results of the former investigation have given a far closer insight into this much vexed question.

I propose first to give the record of cases that I have found which include analytical work, then the cases that came to my notice in which analytical results on wall paper and urine may be compared, and then to discuss the cause of wall paper poisoning in the light of the chemical and biological facts brought out both by this paper and the foregoing.

I have hesitated to introduce the medical side of the cases, but have considered it necessary to the completeness of the paper. The cases are stated, however, either as I found them or as they were given to me. I have further endeavored not to venture any opinion but what might be advanced from the chemical evidence. Whatever may be said of the suggestions offered, the facts are laid before the medical profession for its information and consideration.

HISTORICAL.

Previous to 1886, the cases of chronic poisoning from wall paper in which arsenic has been found in the urine are as follows.

Lorinzer * of Vienna, in 1859, gives the following cases, the analytical work being done by Kletzinsky: —

1. A girl of seventeen had occupied for two years a room of which the walls were colored by Mitis green. The symptoms were loss of appetite, headache, nausea, unquiet sleep, pains in the shoulder, eruption in the knee joint, constipation. The patient was always pale, with sunken cheeks and dark rings under the eyes. She was removed to another room and given potassic iodide, six grains daily, with warm bath twice a week. In two months she was restored to her normal health. The urine was not examined for arsenic.

2. A woman fifty-four years old had occupied for some years a room which was found to have a paint or wash containing quantities

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* Wiener Med. Wochenschrift, 1859, Heften 43 and 44.

of arsenic and copper. In previous years, she had no especial trouble except occasional pains in shoulder joints and back, but in the winter in question these increased, and she began to lose appetite and flesh, and her health was generally bad until she went away for the summer. After her return in improved health, she continued well at first, but came down after a while with fever, with severe pain in the neck and shoulders. The latter left her with the fever, but there remained a peculiar unpleasant feeling, accompanied by pain in the abdomen. She was also troubled by insomnia, which, oddly enough, appeared to be intermittent, a sleepless night being followed by one of comparative rest. Her appetite was poor, but there was no marked symptom of digestive disturbance, and the tongue was not coated. There was dryness and burning in the throat. Constipation was marked. The spleen was not enlarged. 850 c.c. of the urine, after treatment with potassic chlorate and hydrochloric acid, were evaporated to 20 c.c., and the solution, free from chlorine, was introduced into the Marsh apparatus previously tested (time not given) for absence of arsenic. After thirty minutes, a very slight mirror was obtained, which looked like arsenic. The patient was then removed to another room and ten grains potassic iodide given daily. After ten days, the urine was analyzed again, and a much larger and more characteristic mirror was found. The iodide was continued for some time, until the patient grew better and suffered no return of the symptoms. The freedom of the urine from arsenic was not then determined.

3. A woman forty-five years old had had typhus, from which she recovered very slowly, the convalescence being retarded by certain symptoms which were inexplicable. She had no appetite and suffered great distress before meals. The tongue was, however, clean. She had pain in the head, insomnia, was irritable and peevish. Pulse normal. After the patient had been nine weeks in bed and was getting no better, the covering of the wall was analyzed, and arsenic and copper were found in quantity. Fifteen grains of potassic iodide were given daily, and, after some days, the urine was analyzed. The apparatus was carefully tested and the urine residue gave a slight but unmistakable mirror which gave reactions for arsenic. The patient was removed to another room and the iodide continued. The symptoms began to disappear, and in four weeks the patient was entirely well.

4. A girl twenty-four years old had typhus in the autumn of 1857, from which she was recovering. Pulse was normal and tongue clear. Constipation marked. Appetite did not return and patient did not recover strength, but was confined to her bed most of the time. She

was troubled by a ringing in the ears which disturbed her sleep. On removal to the country, her health improved, but on return to Vienna in the following autumn, some of the symptoms returned. There was now some nausea. The throat was red and irritated. The girl had slept for several years in the room, and had apparently not been affected by the arsenic, which was found, together with copper, in quantity on the walls. Twenty grains of potassic iodide were given, and after several days the urine was found to contain a trace of arsenic, as well as a trace of copper. The green coloring matter was removed from the walls. After continuing the doses of iodide, together with warm baths and exercise, the patient in a few weeks recovered.

5. A woman seventy-eight years old had lived for some time in a room the walls of which were colored by Mitis green, which could be easily rubbed off. In the spring of 1858 she was troubled by periodical recurrence of ringing in the ears and tightness in the head, accompanied by digestive disturbance and constipation, and a feeling of oppression in the stomach. On going to the country she became better, but on return in the autumn was necessarily confined to the house, and the symptoms returned. The ringing in the ears was intensified. There was pain in the abdomen, which was distended and painful to the touch. Pulse and respiration normal, skin dry, tongue clean. Nights sleepless and anxious. April 29, 1859, arsenic and copper were found in the urine in traces. Ten grains of potassic iodide were prescribed daily, and for the first few days the symptoms decreased. The ringing in the ears was less and the nights were better. Patient then became feverish, with dry cough and metallic taste. May 15, no arsenic or copper could be found in the urine. During the following days the metallic taste increased, and there was excessive flow of saliva. The iodide was given up and an astringent wash applied, stopping the flow of saliva. May 29, there was again no arsenic in the urine. During this time pleuritis had come on, and it developed into pneumonia, from which the patient died on June 3. Some days before death, the ringing in the ears had stopped, but there was a burning sensation in the stomach day and night, and the patient vomited mucus. The intestines and brain were examined for arsenic, but none could be detected with certainty.

In these five cases, although the details of the analyses are not given as carefully as could be desired, it is probable that a small amount of arsenic was found in the urine, though it was impossible to estimate it with the means then at hand. It is safe, however, from the description of the mirrors, to set a limit of 0.05 mgr. arsenious oxide per litre. The elimination was apparently increased by the potassic iodide, but the rate of elimination was not sufficiently studied.

Müller,* of Augsburg, in 1860, considers Kletzinsky's results to have been not well established, and gives the following cases, which are also detailed by Fabian,† who performed the analytical work.

1. Man, aged 37. Symptoms: headache, loss of appetite, excess of saliva, eructation, oppression after eating and vomiting, tongue slightly coated, constipation. Medicine gave no relief, but absence from home improved his general health. On return symptoms increased, and, in addition, patient complained of pressure on brain and dizziness. The wall paper had been sold as free from arsenic, but contained a large quantity, and the color could be easily rubbed off. Fabian predicted a negative result when asked to analyze the urine. December 13, 1859, after finding his reagents free from arsenic, he established the presence of arsenic in 912 grams of urine. He went over his reagents again with the same result, and an examination of a fresh quantity of urine showed arsenic again. The urine was treated with potassic chlorate and hydrochloric acid, evaporated, precipitated by sulphuretted hydrogen, and the precipitate thus obtained tested in the Marsh apparatus. The wall paper was removed, and potassic iodide prescribed (dose not stated). December 23, 812 grams of urine were analyzed, and a greater quantity of arsenic was found than before, the amounts in both cases being comparatively small. January 19, 1860, 912 grams of urine were found to be completely free from arsenic. This in 37 days after taking the potassic iodide. Recovery followed the removal of the paper.

2–3. A woman, aged 27, and her child, 18 months, had lived for some time in a room which was covered by a green unglazed paper, in which arsenic and copper were found. The mother complained of recurrent headache and pressure in the head. Both were extremely pale and suffered from indigestion. January 28, 720 grams of the mother's urine showed a trace of arsenic, after which the wall paper was removed and potassic iodide prescribed. February 10, 692 grams showed an increased amount. February 27, 716 grams showed a less amount, and on March 27, 62 days after taking the iodide, the complete absence of arsenic was proved.

550 grams of the child's urine, examined January 28, yielded no arsenic. This may perhaps find explanation in the fact that,

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* Wiener Wochenschrift, 1860, Heften 18, 19, 20, 21.

† Dingler, Polyt. Journ., CLVII. 212.

shortly before the examination, the physician had prescribed a powder of lactate of iron, magnesia, and phosphate of lime, which may have had some effect on the elimination. The physician did not dare to try the effect of potassic iodide, owing to the child's constitution. Both mother and child improved after the paper was removed.

This investigation is accurate, and the results reliable. It is unfortunate that no method was known to Fabian which would have permitted the determination of such small amounts of arsenic. From the description of the mirrors, I cannot place the amounts at over 0.05 mgr. per litre.

Kirschgasser,* in 1868, published twenty-one cases of chronic poisoning, chiefly from arsenical wall paint, in which are the most complete details of symptoms that have ever been presented. I need not refer to these cases at any length, as they are well known, and are commented upon especially in Dr. Putnam's paper, above referred to. I note, however, the following. The rooms were partly on the ground floor, partly on the first or second story, and were not damp, though some were badly aired. There was no apparent opportunity for miasma. Occasionally a garlic odor was observed. The children appeared less affected than the elders. In one case, the intermittent character of the symptoms noticed by Lorinzer † was confirmed.

The urine was examined in eight of the cases, with a positive result in six. In one of the two negative tests the urine was not collected until six weeks after the removal of the arsenical color. The work was done very carefully by Holthof. Large amounts of urine (6 to 18 pounds, and in one case 25 pounds) were taken, and the reagents examined in quantities larger than would be used in one analysis. The method of analysis in seven of the cases was as follows. The urine was acidified with hydrochloric acid, and sulphuretted hydrogen was led in for eight days, occasionally warming. The precipitate was collected on a filter, dried, removed from the filter, and evaporated repeatedly with nitric acid. The acid was neutralized by sodic carbonate, and the solution evaporated and melted to destroy all organic matter. The sodic nitrate was then decomposed by sulphuric acid, and the clear solution put into the Marsh apparatus. The reduction tube was heated for 30 minutes, and the mirror examined for arsenic. In the eighth analysis, 25 pounds of urine were acidified with nitric acid and evaporated to dryness on the water bath. The residue was treated with fuming nitric acid and heated until the mass melted quietly, after which it was dissolved in a little water, filtered, and the filtrate heated with excess of sulphuric acid until the nitric acid was expelled. The diluted acid solution was then added to the Marsh apparatus and gave no mirror in 30 minutes. After establishing the absence of arsenic in the urine of the case where six weeks had elapsed before collection of the urine, an analysis was made, two weeks later, of ten pounds of fæces. These were heated two days with dilute potassic hydroxide, and chlorine led in. The brown mixture was decanted from the sediment, saturated with hydrochloric acid, and chlorine passed until quite clear. After driving out excess of chlorine, the solution was treated with sulphuretted hydrogen, and thereafter as in the urine analyses. A heavy mirror was obtained. This is interesting as showing the elimination by the fæces after the elimination by the urine had ceased.

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* Vierteljahr. f. gericht. Med., N. F., IX. 96.

† *Loc. cit.*

In no other case, however, was there any attempt to show elimination of the arsenic, on removal of the cause of poisoning and cessation of the symptoms. The results of the analyses agree with those of Kletzinsky and Fabian in that only small quantities of arsenic were found. The quantitative determination was impossible as before.

Clarke,* in 1873, gives the case of a woman living in a badly ventilated room papered with a highly arsenical paper, who had symptoms which he said might be attributed to a mild case of typhoid fever; great prostration, headache, wakefulness, great nervous excitement, irritable stomach, and coated tongue. An analyst found the dust of the room to contain about 0.2% of arsenic, and in 48 oz. (1,700 c. c.) of urine he obtained 0.26 grain (16.8 mgr.). The sputa contained a trace. Unfortunately, the method of analysis is not given, and we have no means of accounting for the great difference between this amount of arsenic (9.2 mgr. per litre) and the amounts in all the other cases we have to deal with. Yet, in the ordinary quantitative methods, which were the only ones available, 16.8 mgr. is a small amount to determine accurately, and it is quite possible that a serious error was made. This view is supported by the amount of arsenic found in the dust, which is, comparatively, very large.

On removal, the patient grew better, but no further test of the urine was made.

Mörner,† in 1876, gives some analyses of urine which are open to criticism from the method of analysis used. In one case, the wall papers were in several layers, all containing arsenic, the inner more than the outer. The reagents were all tested by a run of 45 minutes, but gave no mirror resembling arsenic. In the first case, four litres of urine were treated with potassic chlorate and hydrochloric acid, but, as the destruction of the organic matter was slow, Schneider's method of distillation with salt and sulphuric acid was resorted to, though no attempt was made, apparently, to reduce the arsenic acid before distillation. The distillate was precipitated by sulphuretted hydrogen, and the precipitate dissolved in ammonia. One half of this solution was evaporated, and the residue examined, according to Fresenius and Babo, by mixing with sodic carbonate and potassic cyanide, and heating in a stream of carbon dioxide. A white mirror was obtained, which on refusion and reheating gave a dark mirror, partially soluble in sodic hypochlorite. In another case, Mörner obtained a "large" mirror. The patient in whose urine this was found went into a room containing no arsenic, and one month later there was no arsenic in the urine. Two other cases gave "smaller" mirrors, another a "doubtful," and in one case there was none. In the urine of people living in rooms containing no arsenic, there was no arsenic found. All the analyses after the first were made by Schneider's method directly.

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* British Med. Journ., June 21, 1873.

† Upsala läkarefören. Forhand., XI. 527; also, ref., Virchow-Hirsch, Jahresb., XI. 405.

One cannot help, on reading Mörner's paper, distrusting the results obtained, as the course of analysis would not only allow arsenic to creep in, but might result in the loss of arsenic, if not carefully conducted. As W. Fresenius* has shown, the Fresenius-Babo method is capable of very delicate work in careful hands, but, in general, it does not give as good results as the Berzelius-Marsh.

Jolin,† in 1880, gives the case of a man occupying a badly ventilated room with an arsenical wall paper, who suffered from recurrent gastric catarrh, conjunctivitis, and great weariness. The urine was treated with potassic chlorate and hydrochloric acid, and evaporated to dryness on the water bath. Potassic nitrate was then added, and the mass warmed with sulphuric acid until nitrous fumes ceased. Into the solution was then passed sulphuretted hydrogen (from calcic sulphide and hydrochloric acid), and the resulting precipitate eventually introduced into the Marsh apparatus. A mirror was obtained 2 cm. long, equally translucent over the entire length, and was judged to be between 0.05 and 0.01 mgr. The reagents were carefully tested, but no mirror resembling arsenic was obtained. Jolin regrets that the amount could not be accurately estimated, but the approximation is probably quite near the correct amount. It is to be regretted that such a long method of treatment was used, as the addition of unnecessary reagents adds to the chances of error.

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* Fresen. Zeitschr., XX. 522.

† Hygeia, Stockholm, XLII. 235.

Welander,* in 1880, reports the case of a man and wife who had been for some time depressed and out of health, especially the woman, who suffered from gastric catarrh. She lost appetite, and became emaciated. Complained of a disagreeable garlic taste, and even imagined that the urine smelled of garlic.† Her depression increased to such an extent that she became hysterical. The papers and hangings were found to be arsenical and were removed, and four days afterward 1,500 grams urine were examined. This was evaporated to the consistency of syrup on the water bath, fuming nitric acid and sulphuric acid were added, and the whole heated on the water bath for twelve hours. The solution was then filtered, and the filtrate saturated with sulphuretted hydrogen (from calcic sulphide and hydrochloric acid) for twelve hours. The precipitate was charred with sulphuric and nitric acids, and the extract added to the Marsh apparatus. After some hours (*sic*) a mirror of arsenic was obtained, mixed with some sulphur. After the removal of the papers, the patient recovered, and, some weeks after, the urine was found to be free from arsenic.

The length of time which elapsed before the mirror appeared renders the result somewhat doubtful, unless there was organic matter or a large quantity of nitric acid in the extract, in which case the reduction of the arsenic would have been retarded. Yet Welander does not say that the reagents received the same long test to assure their freedom from arsenic.

Kjellberg,‡ in 1881, gives the case of a healthy woman, who suffered during the winter of 1878–79 from headache, loss of appetite, and frequent diarrhœa. The wall paper was found to be arsenical. In the summer of 1879 she was restored to health by a journey, and came back to a new house. As the symptoms returned, the surroundings were examined, and the mattress cover was found to contain arsenic. Arsenic was found in the urine, but two months after recovery it was absent.

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* Hygeia, XLII. 238.

† This may, of course, be purely imaginary, but one is reminded of Selmi's claim (see previous paper, page 147) of the discovery of a volatile arsine in the urine of a dog poisoned by arsenic.

‡ Hygeia, XLIII. 456; ref., Virchow-Hirsch, Jahresb., XVII. 398.

Reichardt,* in 1883, mentions a case in which a certain room had been covered for twenty years with a slightly arsenical paper. The occupant had felt no ill effects, but on calcimining over the paper with a green, which proved to contain a quantity of arsenic, symptoms were felt which were attributable to arsenical poisoning. The calcimining was done in damp autumn weather, and the room was used as a work-room until late at night. A garlic odor was noticed. The urine, slightly acidified with nitric acid, was treated with sulphuretted hydrogen for 24 hours, and the resulting precipitate eventually introduced into a Marsh reduction flask. By a method proposed by Reichardt † himself, the gas from the flask was led into argentic nitrate. The latter was then treated with bromine water, the argentic bromide filtered off, and the arsenic acid in the filtrate precipitated by magnesia mixture. A precipitate of ammonio-magnesic arseniate could be detected, but not in sufficient amount to estimate. It must, however, have been less than a milligram, as Reichardt claims to be able to determine that amount by his method.

I am unable to find any other detailed cases in which arsenic was found in the urine up to the beginning of my own work in 1886, although Wood ‡ mentions the fact that he found arsenic in the urine in a case of wall paper poisoning, and I do not know that others had not done the same. In none of the cases, except that of Clarke, has there been any quantitative analysis possible. Yet, with this same exception, the amounts found have been exceedingly small, and in this respect confirm the results obtained by me.

CASES AND ANALYTICAL WORK.

From the results above and my own, it is evident that the amount of arsenic to be looked for in the urine is very small; hence the method of analysis becomes of the greatest importance. Every one knows the wide distribution of arsenic, and unless we can, by the utmost care, shut out the possibility of its getting into our analysis, except through the urine, the value of the analysis is nothing. Not only must the reagents be most carefully tested in quantity greater than likely to be used, but as few reagents as possible must be employed. Dishes and other utensils must be scrupulously clean.

The treatment of the urine in the cases below was as follows. To a measured quantity was added about one tenth of the amount of concentrated nitric acid, and the whole evaporated to dryness over a free flame. As the mass nears dryness, the flame is lowered. More acid may be added if necessary, care being taken to have an excess, in order to avoid carbonization of the mass at the end. Deflagration often ensues, but loss of arsenic is not to be feared in presence of an excess of nitric acid. The organic matter is nearly all destroyed by this treatment, but, to eliminate all, the residue is transferred to a smaller dish, a little more nitric acid and strong sulphuric acid are added, and the whole heated until a clear white melt is obtained, which fumes strongly. After cooling, water is added, and the contents of the dish added to the reduction flask of the Marsh apparatus. The detection and determination of the arsenic are conducted by a modification of the Berzelius-Marsh method, published by me two years ago.* It is only by such an optometric process that the extremely small amounts of arsenic can be quantitatively estimated, the principle of the modification being the comparison of the mirrors with those obtained from definite amounts of a standard solution of arsenious oxide.

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* Archiv d. Pharm., [3], XXI. 271.

† Ibid., [3], XVII. 291.

‡ Mass. State Board of Health Report, 1884.

Thus the reagents used are sulphuric acid, zinc, distilled water, and nitric acid, all of which have been repeatedly tested in larger quantities than would be used in one analysis. The utensils: evaporating dishes of Berlin porcelain, stirring rods, funnels, beakers, and measuring cylinders have been used for this purpose alone. The filter paper has been tested in quantity. Fearing that the glaze of the dishes might contain arsenic, and that the glaze would be dissolved by the acid sulphates, I kept a quantity of melted acid potassic sulphate in a dish for some time, stirring also with the glass rod used. No arsenic was found in the solution, showing that there was no danger from this source. Finally, blank trials with non-arsenical urine, conducted exactly like the others, confirmed the purity of the reagents and the cleanliness of the utensils. In collecting samples of urine, care has been taken to guard against accidental introduction of arsenic from unclean bottles.

The reduction tube of the apparatus is drawn out so as to give two heating places. Before introducing the solution to be tested, the apparatus is run for one hour with the lamp under the first heating place, and the absence of arsenic in the apparatus fully determined. One half, or any aliquot part, of the solution is then added. After 30 minutes, the lamp is moved back to the second heating place, the rest of the solution added, and the heat maintained for 30 to 60 minutes longer. Of the two mirrors thus obtained, one has been used to confirm the presence of arsenic by solution in sodic hypochlorite, or, when possible, by the odor on heating, while the second has been retained for reference. In case the amount of arsenic is too small to divide, the whole may be collected in one mirror.

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* These Proceedings, XXVI. 24.

I have found the careful destruction of the organic matter to be necessary, as a comparatively small quantity of organic matter in the reduction flask is of decided hindrance to the reduction of the arsenic and deposition of the mirror. That this is the case seems to be the general opinion, although Chittenden and Donaldson* state that their results are not affected by the presence of organic matter. They were able to recover from 50 c. c. urine, introduced into the flask directly with a few drops of olive oil to prevent frothing, the original amount of arsenic added, besides getting a distinct mirror from 0.01 mgr. It would, however, be impossible to work with the concentrated solution of a large quantity of urine without destroying the organic matter partially, and I have taken the precaution to destroy it thoroughly, particularly as the use of the method as a quantitative one depends on the uniformity of deposit of the arsenic mirror, and this cannot be assured in the presence of organic matter.

The cases in which the analytical work fell to me are as follows: —

Case 1. In the autumn of 1883, Mr. A. and wife took a house in Cambridge, of which four rooms, parlor, dining-room, study, and bedroom had been recently papered. In the spring of 1885 the halls of the house were covered, and either in 1883 or 1885 the other rooms. These papers contained the following amounts of arsenic calculated as arsenious oxide.

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* Amer. Chem. Journ., II. No. 4.

	Mgr. per Sq. Meter.	Grains per Sq. Yard.
Parlor.	64.9	0.830
Hall.	104.5	1.340
" border.	Very large amount,	not estimated.
Dining-room.	479.0	6.130
Bedroom walls.	96.1	1.230
" ceiling.	1.0	0.013
Study walls.	255.0	3.260
" ceiling.	3.0	0.040
" border.	153.1	1.960
Another bedroom, walls.	0.0	0.000
" " ceiling.	2.0	0.026
" " " border.	596.0	7.630
" " wall "	115.4	1.480
" " frieze.	552.6	7.130
Servants room.	72.8	0.940
Storeroom.	25.2	0.330

The rear hall and bathroom contained small amounts, and were not quantitatively examined. For several months after taking the house no trouble was experienced, but toward the summer of 1884 Mr. A. and his wife, together with a gentleman who occupied the house with them, began to feel some discomfort. This disappeared during the absence of the family from the house in the summer, but began again soon after they returned in the autumn. The plumbing was in good condition and the furnace was a new one. From the fact that the discomfort was worse when the latter was in action, the source of the trouble was attributed to it. No immediate increase of the symptoms followed the papering of the halls, but the health of the family grew worse during the spring of 1885. The chief symptoms were trouble with the digestive organs and insomnia. The tongue was heavily coated, and the food seemed to "sour" in the stomach. Nausea was frequent. There was much languor and dizziness and the eyelids were badly inflamed. In July the family went away to the sea-shore, and there was marked improvement; but on going back to the house for August the symptoms appeared again, while return to the sea-shore for September brought immediate relief. In the early autumn the symptoms returned, but were not at their height until the furnace was used. This was again thoroughly overhauled and the air of the house tested for carbon monoxide with negative results. Mr. A.'s symptoms increased to a greater extent than those of the others, and were accompanied by soreness of the abdomen and abdominal pains at night.

During the last week of December, 1885, the source of the trouble was discovered by a qualitative analysis of the papers. Pending the removal of the papers, the family left the house and experienced immediate relief, especially in sleeping, but many of the symptoms continued for some time afterward. January 7, 1886, a week after leaving the house, 1,750 c.c. of Mr. A.'s urine were analyzed by the method detailed above, and contained 0.01 mgr. arsenious oxide per litre. The papers were replaced by absolutely non-arsenical paper, and the health of the family gradually came to its normal condition, although there was occasional digestive disturbance. The elimination of arsenic from the system was apparently very slow. 800 c.c. of urine, analyzed March 31 (84 days), contained about as much as before, and 820 c.c., analyzed May 26 (140 days), contained 0.007 mgr. per litre. Some time after this another sample of urine was sent to me at Annapolis, and was set aside with several others until I should find time to take up the subject again. So much time elapsed, however, before the analyses could be made, that I do not consider the results worthy of record.

Case 2. Mr. C., aged 25, had for some years slept in a large room, the paper of which contained from 10 to 15 mgr. arsenious oxide per sq. m. (0.13 to 0.20 gr. per sq. yd.). The temperature was low, and there was a good circulation of air in the room. At all events, no ill effects were felt, and the urine, examined during January, 1886, contained no arsenic. July 7, 1886, Mr. C. went to a house at the seashore and occupied a small room, of which the paper contained 146 mgr. per sq. m. (1.88 gr. per sq. yd.). The area of paper was about 22 sq. m. (26.3 sq. yd.). In addition the windows were hung with red curtains about 4 sq. m. (4.8 sq. yd.) in surface, containing 151 mgr. per sq. m. (1.95 gr. per sq. yd.). Soon after taking the room he began to suffer from indigestion with occasional bowel pains. A qualitative analysis of the paper showing arsenic, the urine was examined on July 15, and contained 0.042 mgr. per litre. Mr. C.

continued to occupy the room, but the pain in the bowels became more frequent, and on July 27 diarrhœa set in. July 28, the room was changed for one in which the paper contained 46.8 mgr. per sq. m. (0.6 gr. per sq. yd.), and on the next day Mr. C. was called away.

Returned in a day or two, and occupied the second room with marked improvement, which continued. August 3 (19 days), the urine contained 0.021 mgr. per litre. During the rest of the month there was no recurrence of indigestion except on one day, August 19. The urine of this day was collected, and a sample was also taken some time after leaving the house. Both shared the fate of those mentioned in the previous case.

Though the second room was arsenical, the apparent exemption from its effect was perhaps due to the lesser amount, perhaps to the difference in the compound of arsenic on the walls. The second room was also better aired than the first.

Case 3. Mr. D., after living in a room which contained no wall paper, removed to another house and occupied a room in which the paper, a dark red, contained 110.4 mgr. per sq. m. (1.42 gr. per sq. yd.). About a month after moving, Mr. D. began to be troubled with severe headaches, which were attributed by one physician to change of locality. These headaches continued for some weeks, and in addition there was trouble with the eyes and throat. Another physician suspecting arsenical poisoning, the paper was examined. Other papers in the house contained arsenic but were only qualitatively analyzed, and contained less than that of the room in question. February 12, 1886, the urine contained 0.015 mgr. arsenious oxide per litre. The paper was removed and a non-arsenical paper substituted. Improvement began at once, and the headaches soon disappeared. Here again was an apparently very slow elimination as on June 18 (127 days) the urine contained 0.003 mgr. per litre.

Case 4. Miss E. occupied a room with a light blue paper containing 842 mgr. per sq. m. (10.78 gr. per sq. yd). The windows were hung with blue cretonne curtains, with flowers and leaves in red, yellow, and green, containing 309 mgr. per sq. m. (3.9 gr. per sq. yd.). No symptoms of this case have been given to me except a long continued inflammation of the eyes, continual lassitude and weakness, and trouble with the throat. The patient, a girl in robust health, became weak and nervously prostrated. The urine examined March 10, 1886, contained 0.02 mgr. arsenious oxide per litre. Miss E. was sent away and rapidly improved in general health. The arsenical paper and hangings were removed and replaced by non-arsenical material. No recurrence of the symptoms was experienced on return to the house. Samples of the urine could not be obtained immediately after removal of the paper, or during convalescence, but in October the urine was free from arsenic.

Case 5. Mr. F., for six years previous to 1886, had occupied a large, dry, sunny room, and generally spent sixteen to eighteen hours each day in it. Two or three years before the report of the case, several stuffed birds and animals, preserved by the free application of arsenious oxide, were placed in the room. The wall paper contained 5.7 mgr. per sq. m. (0.073 gr. per sq. yd.), and the border 0.4 mgr. (0.005 gr.). The paper of an adjoining bedroom contained 23.1 mgr. per sq. m. (0.3 gr. per sq. yd.). The analysis of the last was made from a sample taken from the wall, with portions of an old, adhering, underlying paper. Mr. F., for nine months prior to April, 1886, "noticed perceptibly a train of nervous disturbances, as occasional attacks of dizziness and unsteadiness, a feeling of depression, and loss of muscular power. He suffered also from a constant coryza, and a dry cough. He had no gastric or intestinal disturbance." The presence of the birds suggesting a possible explanation of the symptoms, 1,500 c.c. urine were analyzed April 12, 1886, and contained 0.03 mgr. arsenious oxide per litre. The birds were removed and the walls and room cleaned, but the papers were left on the walls. April 26 (14 days) 1,350 c.c. showed 0.026 mgr. per litre. Mr. F. improved in general health after removal of the preparations, but the elimination of arsenic was apparently slow. June 1 (50 days), 1,220 c.c. gave 0.002 mgr. per litre. June 14, Mr. F. began to take five grains potassic iodide three times daily, which seemed, as in the above cases of Lorinzer and Müller, slightly to increase the elimination, as on June 21 (71 days) the amount from 1,320 c.c. was at the rate of 0.006 mgr. per litre. Yet on July 16 (96 days) there was still a trace, 1.270 c.c. giving 0.002 mgr. per litre. This is possibly explained by the presence of the wall papers, or by the fact that the carpets had not been shaken. The iodide was discontinued, and Mr. F. went away for two months, returning "feeling very well physically, the symptoms alluded to having mainly disappeared."

Case 6. This is Case 13, reported by Dr. S. W. Driver of Cambridge, in Putnam's paper.* "The case was one of severe and painful inflammation in the abdominal cavity, with constipation and loss of strength, . . . but it was difficult to say what symptoms, if any, were to be attributed to its [the arsenic] influence."

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* *Loc. cit.*

The only wall paper in the house was in the room where the patient spent a great deal of his time, and the amount was 690 mgr. per sq. m. (8.8 gr. per sq. yd.). The urine, analyzed May 18, 1886, contained 0.016 mgr. per litre, and June 16 (29 days), after removal of the paper, 0.002 mgr. per litre.

Case 7. This is one of the group reported in Putnam's paper by Dr. J. T. G. Nichols of Cambridge, but the analysis of the urine was not given. Dr. Nichols sends the following facts to me: "The girl was about four years of age. She had indigestion, constipation, and occasional vomiting. Insomnia was a marked symptom. She had frequent attacks of sore throat, and was much troubled by eczema of the vulva and anus. She was easily tired and very irritable. She did not lose flesh nor color." The wall papers were examined by Professor H. B. Hill. In the child's room was a blue frieze about six inches wide containing 710 mgr. to the sq. m. (9.09 gr. per sq. yd.). One of the other papers in the house contained 153 mgr. per sq. m. (1.96 gr. per sq. yd.), another 83 mgr. (1.06 gr.), while the rest were but slightly arsenical.

April 6, 1886, 250 c.c. urine gave an amount of arsenic equivalent to 0.015 mgr. per litre. The papers were removed, and "gradual but steady improvement soon began." The elimination was slow, but I cannot say that all arsenical surroundings were removed. On June 29 (84 days), 200 c.c. urine gave 0.012 mgr. per litre, and on July 15 (100 days), 930 c.c. gave 0.008 mgr. per litre. The child had no return of the symptoms after removal of the papers.

The following cases are accompanied by analyses of the papers and a single analysis of the urine.

Case 8. This is Case 10, reported by Dr. Driver, in Putnam's paper. Patient, N. J., a girl aged 17, and her sister (Case 9), occupied a room of which the walls were covered by an old-fashioned paper, with red flowers and green leaves, and bordered with a strip of dark green two inches wide. The green was probably Scheele's or a similar one. The paper contained 116.7 mgr. per sq. m. (1.48 gr. per sq. yd.), and the border 1,200 mgr. per sq. m. (15.36 gr. per sq. yd.). The health of both girls had been impaired for two years. Dr. Driver noted to me the following in N. J.'s case: "Puffed and swollen face, reminding one of the effects of ivy poisoning, anæmia, quick pulse, 80 to 90, dizzy head, nausea, no appetite, dyspepsia. Slight trace of albumen that soon disappeared. Grew better under diuretics and tonics." The urine was analyzed May 5, 1886, and contained 0.068 mgr. per litre. On removal of the paper, recovery ensued.

Case 9. (Case 11, Driver-Putnam.) M., aged 19, sister of N. J., occupied same room, but was away from home during the day, while her sister N. remained at home, made the beds daily, and swept and dusted the room once or twice each week. Dr. Driver notes symptoms: "Dyspepsia, irritated eyes for which she went to the eye and ear infirmary, poor appetite, recurring pustules in outer meatus of ear. Would feel wretchedly for two or three days at a time." The urine, examined May 5, contained 0.028 mgr. per litre. The difference in amounts is interesting, from the fact that M. spent less time under the influence of the paper than N. did, and that she was less affected. As in the case of her sister, recovery followed the removal of the paper.

Case 10. Miss G., aged 30, occupied a small room in a seaside hotel, the paper of which contained 185 mgr. per sq. m. (2.37 gr. per sq. yd.), and the border 134 mgr. per sq. m. (1.72 gr. per sq. yd.). The areas of paper and border were, respectively, 27.7 sq. m. (33.08 sq. yd.) and 1.86 sq. m. (2.22 sq. yd.). Connecting with this room was another, on which was 23.4 sq. m. (27.95 sq. yd.) of the same paper and 1.86 sq. m. (2.22 sq. yd.) of the same border. For about a month after taking the room, the occupant was never free from indigestion. There were occasional severe pains in the bowels with constantly recurring diarrhœa. The first room had but one window and the circulation of air was poor. The occupants of the second room were apparently not affected, but it must be taken into account that this room had three windows and was well aired. The walls of both rooms were covered with a glue "size," and the symptoms soon began to abate. The urine was not obtained until six days after the size was put on. It then contained 0.054 mgr. per litre. During the rest of the summer no return of symptoms occurred except occasional slight indigestion.

Case 11. S. H., a girl aged six, had occupied for over a year a room of which the paper contained arsenic, but the amount was not determined. During the spring of 1886 the child began to show a capricious appetite, with signs of digestive disturbance. The family took a house at the seashore on July 3, and S. occupied with her brother (Case 12) a room on the lower floor, the paper of which contained 313.5 mgr. per sq. m. (4.01 gr. per sq. yd.), the border containing 128 mgr. (1.63 gr.). No other symptoms were developed, but the indigestion became more marked. August 7, 860 grams of the urine contained 0.019 mgr. per litre. On this day both children were removed to a communicating room, merely for a change, the difference in the amount of arsenic not then being established. Little or no improvement resulted. The paper in this room contained 109 mgr. per. sq. m. (1.41 gr. per sq. yd.), and the border had 24 mgr. (0.31 gr.). August 12, both rooms were sized with glue. The effect was soon noticed and the child improved rapidly.

Case 12. T. H., brother of S. H., aged four, had occupied a room which contained but a trace of arsenic in the wall paper, and on coming to the sea-shore house was perfectly well. Occupied same room as his sister (Case 11), but no signs of a similar digestive disturbance showed themselves. August 7, he was removed with his sister to the communicating room. About this time he had been playing during the day with a red flag which was afterwards found to contain 336 mgr. per sq. m. (4.08 gr. per. sq. yd.), and he kept it with him for several days. August 9, he was attacked with diarrhœa, accompanied by fever, which lasted for three days. The urine contained 0.008 mgr. per litre. August 12, as mentioned above, both rooms were glue sized, and for the rest of the summer there was no further trouble.

The other papers in the house were, with one or two exceptions, highly arsenical.

Case 13. Mr. J., a clergyman in good health, lived in a house which was papered in the spring of 1885. Three of the papers contained arsenic in considerable quantity; study, 40.6 mgr. per sq. m. (0.5 gr. per sq. yd.); bedroom, 31.2 mgr. (0.4 gr.), and the third, which I believe covered the hall, 14.4 mgr. (0.18 gr.). Not long after the rooms were papered, Mr. J. began to suffer from extreme languor and diarrhœa, for which he could discover no satisfactory cause, either in diet or daily habits. These continued until he left home for his vacation, and for six weeks he was in perfect health. On return, the symptoms came back, accompanied by insomnia, dyspepsia, and swelling of the hands and feet. Neither his local physician nor a New York physician whom he consulted could assign a cause for what seemed to them to be a case of poisoning. The analysis of the urine, February 25, 1886, showed 0.01 mgr. to the litre. The walls were stripped and the patient "treated for arsenical poisoning." Mr. J. reported his health to me afterward as being improved, but, as he was unwilling to pursue the matter further on account of publicity, the record ceases here.

Case 14. This case was reported to me by Dr. A. P. Clarke, of Cambridge, and mentioned by him at the meeting of the South Middlesex Society above referred to. Mrs. L., aged 51, occupied for seven years a tenement, of which the papers, most of them quite old-fashioned, contained the following amounts of arsenic.

	Mgr. per Sq. Meter.	Grains per Sq. Yard.
Bedroom.	4.5	0.06
Room next bedroom, where patient occasionally sat.	611.7	7.83
Front and back parlor.	87.2	1.12
Kitchen.	51.0	0.65
Hall.	7.8	0.10
Dining-room.	23.1	0.30

For several months Mrs. L. had suffered with severe neuralgic pains, "accompanied, from time to time, by a good deal of constitutional disturbance." There was much gastric disturbance, with frequent attacks of nausea and vomiting. On removal to another house she began to improve and was getting much better, until, contrary to the physician's advice, she occupied a room of which the paper was arsenical (not sent to me for analysis). A return of the symptoms followed. When she finally took a room in which the papers were examined and found free from arsenic, she began to get better again, and since then had not shown any signs of a relapse. The urine, taken 60 days after removal from the first house, contained 0.01 mgr. per litre.

In the following cases the wall papers were not submitted to me for analysis:

Case 15. (Drs. Putnam and Driver, Case 14.) "The patient, being a lady of 58, showed, besides the more common symptoms of impaired nutrition and digestion, numbness of the hands at times and weakness in walking. In the presence of these symptoms, it is fair to suspect that a searching physical examination of the muscles, and of the sensibility of the skin might have justified a diagnosis of neuritis. Without that, the numbness of the hands at least can only be counted as a corroborative symptom. The source of the arsenic was not traced, but the patient improved on leaving home and relapsed on her return." 370 c. c. urine were analyzed July 14, 1886, and the amount of arsenic found was 0.005 mgr. per litre.

Case 16. (Drs. Putnam and Driver, Case 15.) "The patient suffered from 'epileptic vertigo,' which was not, however, attributed to the arsenic. She had also obscure digestive and nervous symptoms. The suspected paper was not removed, and the patient did not recover." 750 c. c. urine, July 1, 1886, gave 0.005 mgr. to the litre.

Case 17. (Drs. Putnam and Driver, Case 16.) "A variety of serious symptoms were present, referable to the nervous system and general nutrition, but Bright's disease was present, and for this reason it would not have been thought worth while to report the case, but that it is a question to be investigated whether arsenic may not occasionally set up a chronic nephritis. The source of the arsenic was not discovered." 1,080 c. c. urine, July 1, 1886, gave 0.055 mgr. per litre.

Case 18. (Drs. Putnam and Driver, Case 17). "Was that of a school teacher, thirty-six years old, and in a rather nervous and debilitated state through her work, without, at first, any distinctly characteristic signs of arsenical poisoning. During the summer months immediately following this period, she spent most of her time out of doors, and also changed her room, and seemed on the high road to recovery. In October, she returned to her former room, and immediately her old symptoms came back, and she was obliged to keep her bed, suffering from ringing in the ears, sleeplessness, attacks of colic at night, followed by diarrhœa, bad taste in the mouth, flatulent dyspepsia, irritation of the eyes and throat, and numbness of the hands. On account of the character of the symptoms, and because they became worse after the house was closed for a time and the furnace lighted, arsenic was suspected and sought for. The paper in the room was found to contain only a trace, but a frieze 20 inches wide and extending through three stories, gave 15 grains per square yard, and it was observed that the hallway formed a sort of shaft through which the heated air was conducted to the patient's bedroom, which was protected only by a portière, with an open space at the top. Furthermore, a small trunk room, the door of which opened next to hers, and which was used, with its window open, to ventilate her room, had an old paper with border and figure of Paris green. . . . The paper has been removed and the patient's gastric symptoms and sleeplessness are much relieved, though she is still under treatment." July 25, 1886, 760 c.c. of the urine contained 0.018 mgr. arsenious oxide per litre.

Case 19. (Drs. Putnam and Driver, Case 12). "Was interesting from the fact that here also were periodic attacks of gastralgia, occurring this time at night, but in addition occasional outbreaks of colic and diarrhœa. Insomnia and debility were also present. There were no other especially characteristic symptoms." May 26, 1886, 960 c c. urine gave 0.01 mgr. per litre.

Case 20. This case was also reported to me by Dr. Clarke. Mrs. D., aged 66, had lived in her tenement for nine years. During this time the rooms were papered in different years with papers which, in eight cases, were arsenical (not sent to me for analysis). "General weakness and nervous prostration have been pronounced symptoms of her case. The mouth and throat have been sore. The parts smart and sting, and the sensations extend into the trachea and œsophagus. The tongue is red, especially at the tip, the follicles are large, red, and protrude, and are very sensitive." On leaving the house for a short time, relief was immediate, but the symptoms reappeared on return to the house. July 2, 1886, the urine contained 0.005 mgr. per litre.

Discussion.

In all these cases the amount of arsenic eliminated by the kidneys is extraordinarily small, varying from 0.002 mgr. to 0.068 mgr. per litre. In the cases quoted in the historical sketch, the amounts could not have been much in excess of this, and in the analyses of Worcester given in Putnam's paper below, the quantity varied from 0.005 to 0.1 mgr. per litre.

I have been able to find but one quantitative determination of the rate at which small amounts of arsenic are eliminated. Hubbard,* in 1882, gives the following experiments. $\frac{3}{50}$ grain (3.87 mgr.) of arsenious oxide was given to a man, in pill form, for five days, and the urine of the last three days collected. On the third day no arsenic was found, on the fourth, 0.01 grain (0.65 mgr.), and on the fifth, "traces." Continuing, $\frac{6}{50}$ grain (7.74 mgr.) was given for two days, then $\frac{4}{50}$ grain (5.16 mgr.) for two days. On the eighth day, $\frac{1}{58}$ grain (1.12 mgr.), and on the ninth, $\frac{1}{83}$ grain (0.78 mgr.), was recovered. During this time the man was indoors and took no exercise. In the second case $\frac{5}{50}$ grain (6.45 mgr.) was given for six days to a man who took sufficient exercise each day to induce fatigue. On the fifth day $\frac{1}{110}$ grain (0.59 mgr.), and on the sixth day $\frac{1}{187}$ grain (0.35 mgr.), was recovered, the urine of the first four days not being examined. In the third case, the person was in feeble health and suffered from indigestion due to gastric catarrh. $\frac{3}{60}$ grain (3.24 mgr.) was given for six days, and on the sixth day no arsenic could be found. Then $\frac{6}{60}$ grain (6.48 mgr.) was given for six days more, and on the twelfth day $\frac{1}{125}$ grain (0.52 mgr.) was recovered. No attempt was made in any of the trials to follow the elimination until it stopped.

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* Physician and Surgeon, Ann Arbor, IV. 348; also, Contrib. Chem. Lab. Univ. Mich., I., Part 1.

When we consider that the determination of the arsenic was made by weighing the mirror obtained, and that the amounts varied from 0.35 mgr. to 1.12 mgr., the chances for error in weighing will be seen to be very great. Furthermore, the evaporated urine was added directly to the reduction flask, and Hubbard himself thinks that the organic matter is apt to interfere with the reduction and accurate deposition of the arsenic.

This, besides being the only quantitative series of experiments that I can find, concerns only the elimination when the arsenic is taken as arsenious oxide.

As to the rate of elimination, then, in cases of chronic wall paper poisoning, there are, so far as I know, no other data than in my experiments or in those of the historical sketch. Wood* has, however, recently made an investigation into the length of time required for elimination in cases where the poisoning occurred from other causes. His results are not quantitative. Two of the cases were chronic (from Fowler's solution), the third being acute (from arsenious oxide). In the first two, 58 and 82 days were required, and in the third 93 days. Wood also refers to a chronic case by Gaillard † (Fowler's solution), in which 53 days were required. In the cases given above, though the elimination was not examined to completion, the time after which arsenic still appeared varied from 19 days to 140 days.

But neither Wood's nor Hubbard's work enables us to draw an inference as to the rate of elimination from such minute doses as would come from a wall paper, and we have no parallel work whatever on the amount or rate when the arsenic is in the form of a derivative of arsenic acid.

In discussing the source of chronic wall paper poisoning, we have to consider in what state the arsenic compounds exist in the air of the room. The possibilities are two: a gaseous or volatile compound, and the solid particles mechanically detached from the paper. In addition to the action of the arsenical dust in the air, we are now in a position to consider the action of a volatile arsenical compound. The formation of a volatile compound from decaying arsenical matter, first discovered by Hamberg,* is now assured beyond question by the results of Gosio,† which I have confirmed, as shown in the foregoing paper. We have, then, either or both of these sources from which the arsenic can enter the system. Let us now consider the first of these.

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* Bost. Med. Surg. Journ., CXXVIII. 414.

† Ann. d' Hygiène, October, 1874.

As the amount of arsenic eliminated is so small, the amount ingested must be also small. As far as I can discover, no experiments have been made to investigate the action of *minute* quantities of arsenic when taken into the stomach, nor do I know of any work on the effect of inhaling air charged with minute particles of an arsenic compound. Furthermore, I have found no information on the action of minute quantities absorbed through the skin and mucous membranes. Thus we have no data to guide us to any conclusion as to the effect of *minute* quantities, however ingested. Yet, as in the case of larger quantities, the toxic effect is better known when taken into the stomach, we may use this channel as a basis of comparison while considering the reason for the action of minute quantities.

But little thought has been given to the compound, or to the state of oxidation in which the arsenic exists in the paper. We may divide the compounds into the trioxide and its derivatives, the pentoxide and derivatives, and the sulphides. Of the former the basic arsenite (Scheele's green) and the aceto-arsenite of copper (Schweinfurth, Paris, Mitis green) were formerly very common, but are now rare in wall paper, though they may appear in domestic fabrics. We may have also the trioxide itself, and possibly a few other arsenites. The sulphides may occur occasionally. But in a very large number of the papers of to-day which contain arsenic the higher oxidation state is found. The use of arsenic acid in the manufacture of rosaniline is liable to leave arsenic in the color as an arseniate, as well as arsenite, while the use of the arseniates as mordants is very common, especially in fabrics.

The effect of arsenious oxide and its derivatives may be inferred to a certain extent from the well known action of larger amounts, but in the case of the action of minute amounts of the sulphides and arseniates we have little to guide us. I have found a few cases of poisoning from arseniates, but, with one exception, a case of poisoning by potassic arseniate,[*] the chemical tests show the substance to have been an arsenite.

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* Pharm. Journ. and Transactions, [3], V. 81; Pharm. Zeitschr. f. Russland, XXV. 779.

† Azione di Alcune Muffe sui Composti Fissi d'Arsenico, Roma, 1892.

The difference in action between arsenious and arsenic acids was first studied by Wöhler and Frerichs[†] in 1848, arsenic acid previous to that time having been considered more poisonous than arsenious acid. They concluded that the arsenic acid was less active than the arsenious, following the analogy of the phosphoric and phosphorous acids. They thought that the arsenic acid was reduced in the organism to arsenious acid. They also proved the poisonous quality of calcic arseniate, although it is insoluble. This is also shown by Schmidt and Bretschneider.[‡] Schroff,[§] in 1852, experimented more carefully than Wöhler and Frerichs, and came to the conclusion that arsenic acid was not very much less poisonous than arsenious acid. Marmé,[||] in 1875, quotes Savitsch,[¶] who found that the poisonous qualities stood in the same ratio as the percentage of metallic arsenic in each. Marmé, however, in a carefully conducted series of experiments, was able to show that arsenic acid is much the less energetic. Reichardt[**] remarks the necessity of determining the state of the arsenic, in order to know whether it is injurious or not. He considers that arsenic acid may be combined with iron in ochres, and supposes ferric arseniate to be harmless. Yet if calcic arseniate is poisonous, why not ferric?

If arseniates are less poisonous in large doses, is it because they are less of an irritant? If less irritating, could they be accumulated more easily if in minute doses?

This leads to the consideration of the localization of arsenic in chronic cases. Scolusuboff,[††] in 1875, found the deposition, when taken as arsenious oxide and sodic arsenite, to be chiefly in the brain, "from which it is carried by the circulation to other organs." Ludwig,[‡‡] in 1881, finds this assertion to be wrong as far as arsenious oxide is concerned, the brain containing comparatively little, while the liver contained the most and held it longest. This view is confirmed by Guareschi,* Bergeron, Delens, and L'Hote,† and Johnson and Chittenden.‡ Chittenden § gives an exhaustive analysis of a body, with quantitative results as far as he could go by his method. The largest amount of arsenic was in a muscle from the back, next in the intestines, and next in the liver. The kidneys contained very little, the brain somewhat more than the kidneys. Chittenden was of the opinion that a marked difference was made in the distribution according to whether the arsenic was given in one dose or in several.

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[*] Bouley, jeune, Mém. Acad. Roy. de Méd., Paris, 1835, IV. 298-307.

[†] Ann. d. Chem. u. Pharm., LXV. 345.

[‡] Moleschott's Untersuchungen, 1859, VI. 146.

[§] Archiv f. phys. u. path. Chem. u. Mikr., Wien, V. 241.

[||] Nachr. v. d. könig. Gesells. d. Wissens. a. d. Georg. Aug. Univ., Göttingen, 1875, p. 614.

[¶] Dissertation, Dorpat, 1854.

[**] *Loc. cit.*

[††] Archiv de Phys. norm. et path., 1875; also, Ann. d'Hygiène publ. et de Méd. légale, Jan., 1876.

[‡‡] Jour. de Pharm. et de Chemie, [5], VI. 198; also, Chem. Centralblatt, 1881, p. 90.

All this work, however, with the exception of Scolusuboff's, has to do with arsenious oxide alone. There is no evidence to show that the same rate or place of distribution holds good for other compounds of arsenic, especially for the arseniates, and we also have no means of knowing where the arsenic goes when ingested in minute, continued doses.

Schmidt and Bretschneider ‖ investigated the question whether the urine contained arsenious or arsenic acid when the arsenic was taken as the trioxide. Their method was somewhat unsatisfactory. Arsenic acid was found and no arsenious, but possibly with a better method they would have found arsenious acid also. Yet the arsenic acid was undoubtedly in excess. Would a minute quantity of an arseniate pass eventually into the urine with less acute disturbance? In the same investigation the above authors examined the effect of metallic arsenic when taken in a perfectly pure state, and found it to cause no acute poisoning. Metallic arsenic was found in fæces and urine. This work was a repetition of that of Schroff,¶ who, using impure material had found metallic arsenic to be poisonous.

A statement of the facts we now possess in regard to the volatile compound is in order here. A brief *résumé* of Gosio's work on this subject has been recently given by Shattuck.**

The compound is generated by the action on arsenical organic matter of the following moulds: *Penicillium brevicaule*, *Mucor mucedo*, *Aspergillum virens*, and *Aspergillum glaucum*, a few others having been found which have a slight action. Of these the most intense action is caused by the first, a mould discovered on decaying paper, though *Mucor mucedo,* which is more widespread than the first, is only a little less active. The conditions for development of the compound by these moulds are moisture, a temperature from 15 to 35° C. (60–95° F.) and a supply of oxygen, without which no action takes place. A large amount of arsenic retards the growth, which goes on best in a ground containing 0.01 to 0.05%. The best nutritive material is a carbohydrate. The development may take place in presence of arsenious oxide or its derivatives, or of arseniates, though the latter seem to me to have given the best results. Little or no action is obtained from the sulphides.

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* Gazzeta Chim. Italiana, XIII. 176.

† Ann. d'Hygiène publ. et de Méd. légale, [3], III. 23.

‡ Amer. Chem. Journal, II. 232.

§ Ibid., V. 8.

‖ *Loc. cit.*

¶ Zeitschr. der Wiener Aerzten, 1858, I. 4.

** Bost. Med. Surg. Journ., CXXVIII. 540.

As to the nature of the volatile compound it was thought from the work of Hamberg and the speculations of others to be arseniuretted hydrogen, an assumption that has been very misleading. Certainly very little, and I think none, is formed. As far as the results go, the compound seems to be a neutral organic derivative, and my opinion is that the results favor its being an organic derivative of arsenic pentoxide. No definite properties beyond its peculiar alliaceous odor and volatility have been found, except that the yellow compound noticed by Hamberg, Gosio, and myself may be a "molecular" compound with argentic nitrate.

It may be remarked in passing that the proof of the formation of a volatile compound is a complete explanation of the poisoning in many cases where an arsenical paper underlies one that is free from arsenic. Also, though the effect of an arsenical paper may be temporarily lessened by a varnish or size, that the danger is not removed.

With the volatile compound we have to consider the question not only of more minute doses than in the case of dust, but of a form which permits the arsenic to enter the system more easily by the lungs and in a state differing greatly from any dust. Whether we have a derivative of arsenious or arsenic acid, the fact that the molecule contains carbon is a very important one.

The experiments of Schröter * on the poisonous action of p-benzarsenic acid, $C_6H_4(CO_2H) . AsO(OH)_2$, are interesting here, though it is not likely that the volatile compound is an aromatic derivative. Schröter found that the amount of arsenic in a fatal dose of benzarsenic acid was somewhat larger than in a fatal dose of either arsenic or arsenious acids, but that death followed after a much longer interval than with either of the others. The early symptoms were referable to benzoic acid, the later to arsenical poisoning.

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* Inaug. Dissert., Erlangen, 1881.

In chronic poisoning a tolerance was established to such an extent that five times as much could be given as would be fatal to an animal not accustomed. In the urine immediately after ingestion an arsenical organic acid other than benzarsenic acid was found, but could not be detected afterward, though the urine was arsenical.

Schröter ascribes the difference in action between benzarsenic and the two inorganic acids to the carbon in the molecule, a separation into benzoic acid and arsenic acid having to be made before the latter can act.

Selmi* claims to have isolated from decaying arsenical animal matter an arsenical alkaloid and a ptomaine, and Husemann,† on the strength of this, thinks that an arsenical ptomaine may be formed by the decomposition of arsenical paste by mould. There is no evidence, however, to show that the volatile compound is of the nature of a ptomaine.

An important contribution to the knowledge of chronic wall paper poisoning was made about three years ago by Putnam,‡ who collected a number of samples of urine mainly from hospital patients, selecting chiefly those cases in which there were no symptoms referable to arsenical poisoning. These samples, 48 in number, were analyzed by Dr. C. P. Worcester, and traces of arsenic found in 21 (44%). A year later,§ Putnam added to this list, making the total number of samples 150, of which Worcester found over 30% arsenical. The method of analysis used was similar to that described in this paper. These results prove the wide distribution of arsenic in articles of household use, and show also that the system is evidently capable, in many cases, of absorbing and eliminating minute quantities of arsenic where a large quantity would act as an irritant.

The following facts may now be noted : —

1. The distribution of arsenic in articles of domestic use is very wide, and it has been shown that it finds its way into the system in many cases where there is no poisonous effect.

2. It is now pretty conclusively shown that arsenic may be in some cases accumulated, instead of always being readily eliminated.

3. The amount of arsenic absorbed in chronic wall paper poisoning may be very minute, but it is in continued doses.

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* Mem. d. Accad. d. Scienze, Bologna, [4], I. 299.

† Arch. d. Pharm., CCXIX. 415.

‡ Bost. Med. Surg. Journ., CXXII. 421.

§ Ibid., CXXIV. 623.

4. The elimination of the arsenic by the kidneys in wall paper poisoning is very slow and the amount eliminated very small.

5. The absorption of the volatile compound, though in smaller amounts, is more direct than that of the dust particles, and the action is modified by the presence of carbon in the compound.

6. The effect of minute doses of any compound of arsenic, in whatever way ingested, has not been studied.

7. The effect of any quantity whatever of many compounds of arsenic that occur in wall papers and fabrics, notably arseniates, is not well known, whether the arsenic compound be taken at once or in continued doses.

8. The localization of any compound of arsenic and particularly of the arseniates, when taken in minute continued doses, has not been studied.

9. The salts of arsenic acid seem to be less irritating than those of arsenious acid. Is this because the state of oxidation permits its readier accumulation?

My position does not permit me to advance any decided opinion on the source of chronic wall paper poisoning, and I can only submit the above facts for consideration. From the facts, however, that have come to my notice during the preparation of these two papers, I cannot help making the following suggestion: —

Chronic arsenical poisoning from wall papers and fabrics may be chiefly due to the ingestion of minute continued doses of arsenic as a derivative of arsenic pentoxide, which from its state of oxidation is likely to be accumulated in the system, from which it is slowly eliminated. The absorption may be from an inorganic arseniate in the form of dust, or from a volatile organic derivative of arsenic acid, or from both.

The remark of Dragendorff,* that a part of the arsenic acid may go into the bones in place of phosphoric acid, should be remembered here. It seems quite possible that calcic arseniate, being isomorphous with calcic phosphate, should replace a part of the latter. This may be confirmed by Ludwig† and Gibb,‡ both of whom found arsenic in the bones, Ludwig finding that it was held there long after the doses ceased. Evidently a large field of investigation must be cleared before a definite conclusion can be reached as to the cause of chronic wall paper poisoning.

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* Ermittelung v. Giften, 1876, p. 326.

† *Loc. cit.*

‡ Trans. Pathol. Soc. London, 1858, IX. 442.

In conclusion, it must be remarked that both Gosio's and my work have shown that a very small amount of arsenic may be quite as good a source of the volatile compound as a very large amount. Hence the limit that can be set as a dangerous amount of arsenic in a wall paper is a matter which should be very carefully considered. It has been thought by many that a paper containing under 0.1 gr. per square yard (8 mgr. per sq. m.) was harmless. If the arsenic were given off as dust alone, perhaps this limit would be sufficient, but, with the chance for the formation of the volatile compound, we cannot, I think, say that 0.1 gr. per square yard is harmless. The matter of limit emphasizes the need of a quantitative analysis of the paper. By the process I have described and referred to here, this is a simple matter, and every paper should be reported, not in the indefinite "traces," "large amounts," "dangerous quantity," etc., but with the approximate figures, so that the physician may *himself* decide as to whether the paper should be rejected or not.

WASHINGTON UNIVERSITY CHEMICAL LABORATORY,
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